Our study clearly showed that mirth was represented in the inferior temporal gyrus, and was closely linked with a particular context (a certain tune in this patient). This association with a specific event was not observed in the patients reported by Arroyo *et al*.[2] Because the temporal lobe is involved in memory function in human, it is reasonable that both the context of the mirth and laughter and the induced mirth and laughter are represented. In the present case, we could not identify any site where the electric stimulation elicited laughter without mirth. Importantly, the fact that the stimulation with higher intensity and longer duration elicited mirth with laugher more effectively suggests different thresholds for mirth and laughter, postulating a hierarchical organisation or serial processing of mirth and laughter in the human temporal cortex. Laughter might be situated at a higher order than mirth, at least in the temporal neocortex. It is possible that laughter might be caused by further activation of the frontal motor cortices, including the anterior cingulate gyrus, through corticocortical projections, such that electrical cortical stimulation could elicit laughter without mirth.[2]

With regard to the characteristics of induced mirth in this patient, the melody which made her feel funny was not amusing by itself in the absence of electrical stimulation, raising the possibility that stimulation changed the internal standard of her amusement through an undetermined process.

Although it should be taken into account that the mirth elicited in the present case might not necessarily have reflected the representation of mirth and laughter in the normal brain, no mirth was seen during the patient's habitual seizures, and neither electrode A4 nor electrode A12 was included in the epileptogenic foci. Thus this particular area (A4–A12) producing mirth on stimulation can be judged to reflect normal function in this patient.

In the present case, mirth is represented in the temporal lobe and may be stored together with the context inducing mirth in the same area, suggesting a close relation between mirth and memory function. As far as the temporal neocortex in the present patient is concerned, laughter seems to be situated at a hierarchically higher order than mirth.

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How valid is the clinical diagnosis of Parkinson's disease in the community?

In a population based study on the prevalence of Parkinson's disease in London, Schrag *et al* reported on the data of a long term clinical evaluation of 202 patients.[1] The initial diagnosis of probable Parkinson's disease was later confirmed in 83%, plus 2% each with atypical features and possible Parkinson's disease. In 15% the initial diagnosis was later rejected, while 19% of patients not diagnosed as Parkinson's disease were later found to have the disorder. Their conclusion was that in 15% of the cases the clinical criteria of Parkinson's disease were not followed, in accordance with previous retrospective clinicopathological studies of parkinsonism, in which the rate of false positive diagnosis ranged between 22–24%[2 3] and 15–18%.[4 5] Using more strict diagnostic criteria by movement disorder experts, this figure could recently be further reduced to around 10%, with a positive predictive value (PPV) for idiopathic Parkinson's disease of 98.6%, and for other parkinsonian syndromes 71.4%—for example, for multisystem atrophy (MSA), 85.7%, and for progressive supranuclear palsy (PSP), 80%.[6 7]

Referring to these data, Schrag *et al* suggested that at least 10% of the patients with a final clinical diagnosis of Parkinson's disease may have other disorders.[1] In pathological series, the incidence of atypical parkinsonism is substantial; for example, PSP is found in 6–22% of necropsy cases, MSA in 5–11.4%, vascular parkinsonism in 2–3%, and Alzheimer's disease in demented Parkinson's disease patients in 2–6%[5 6] (see table 1).

Although samples from brain banks and specialised institutions are considered to overrepresent atypical disorders owing to the referral bias inherent in such samples,[7] these data are, at least in part, confirmed by a large consecutive clinicopathological study of 260 elderly patients with a clinical diagnosis of parkinsonism derived in the years 1989 to 2001 from three large community hospitals in Vienna, two with acute and one with chronic care facilities (table 1). The concordance of the clinical diagnosis with the necropsy findings in this cohort was much better than in previous series[5] (table 2), which, unfortunately, was not considered or quoted by Schrag *et al*. In our recent necropsy series, the mean incidence of Lewy body disease, including Parkinson's disease, was 78%; of other neurodegenerative disorders masquerading as Parkinson's disease (for example, PSP, MSA, and so on), around 12%; while other disorders referred to as secondary parkinsonism (essential tremor, drug induced parkinsonism) accounted for 8.4% (table 1). The initial rate of misdiagnosis in the overall group of 750 cases was around 17%, and, owing to more precise diagnostic criteria, this finally fell to 11.5% (table 2).

A review of the clinical and pathological diagnoses of 160 non-demented patients with parkinsonism (85 men, 75 women; mean (SD) age, 76.6 (8.3) years, range 52 to 96)—the majority of whom had been examined in hospitals by neurologists experienced

Table 1 Incidence of different types of Parkinsonism in necropsy series (percentages)

	Schrag *et al*[1] (clinical PD)	Hughes *et al*[2]	Jellinger[5] (1957–70)	Jellinger[5] (1971–88)	Jellinger (1989–2001)	
					n	%
Idiopathic Parkinson's disease	61.4	50.0	75.3	77.0	151	57.6
(Brainstem LB disease)	(2.0)					
Lewy body dementia		–	2.7	5.8	53	20.4
Lewy body disease (total)			78.0	82.8	204	78.0
Other degenerative parkinsonism		33.0	10.0	8.9	34	13.2
Multiple system atrophy	1.5	22.0	4.6	2.3	9	3.5
Progressive supranuclear palsy	3.0	11.0	3.6	2.6	8	3.1
Pick disease, corticobasal degen	–	?	0.9	0.5	2	0.8
Alzheimer's disease	–	?	0.9	3.5[a]	15	5.7
Secondary parkinsonism		17.0	12.0	8.3	22	8.4
Vascular parkinsonism (MIE, SAE, MIX)	5.5	?	3.0	4.2	8	3.1
Postencephalitic parkinsonism	–	?	6.3	1.9	0	0
Symptomatic (JCD, tumours, etc)	3.5	?	0	0.3	3	1.1
Toxic/drug induced parkinsonism	–	?	0.9	0.3	3	1.1
Post-traumatic/boxer dementia	–	?	0.9	0.3	0	0
Unclassified/no lesion ("tremor")	22.8	?	0.9	1.3	8	3.1
Total	**202**	**143**	**110**	**380**	**260**	**100.0**

[a]With SN lesion 3.0.
JCD, Jakob-Creutzfeldt disease; LB, Lewy body; MIE, multi-infarct encephalopathy; MIX, Alzheimer's disease plus vascular encephalopathy; PD, Parkinson's disease; SAE, subcortical arteriosclerotic encephalopathy.

Table 2 Misdiagnosis in necropsy series of clinical Parkinson's disease (with or without dementia)

Pathology	Hughes *et al*[2] (n=100)	Rajput *et al*[3] (n=41)	Jellinger (1971–88)[5] (n=380)	Jellinger (1989–2001)[5] (n=260)		Hughes *et al*[6] (n=143)
				n	%	
Alzheimer's disease	6	2.0	2.6	5	1.9	?
Vascular encephalopathy	0	2.0	3.5	2	0.8	?
Progressive supranuclear palsy	8	0.0	1.8	3	1.1	3.5
Multiple system atrophy	5	10.0	2.2	3	1.1	3.0
Nigral atrophy (unclassified)	2	2.0	0.5	1	0.4	
MIX encephalopathy (AD+VaE)	0	0.0	0.5	1	0.4	
Lewy body dementia	1	0.0	3.6	12	4.6	
Pick's disease, corticobasal degeneration	0	0.0	0.2	0	0	8.7
Normal (essential tremor?)	1	0.0	0.3	2	0.8	
Others (pallido-nigral degeneration, toxic, etc)	0	2.0	0.3	1	0.4	
Postencephalitic parkinsonism	1	4.0	0	0	0	
Total	**24**	**22.0**	**15.3**	**30**	**11.5**	**15.2**

Values are % unless stated.
AD, Alzheimer's disease; VaE, vascular encephalopathy.

in movement disorders over a 12 year period from 1990 to the end of 2001—gave the following results: 129 were clinically diagnosed as probable idiopathic Parkinson's disease without severe dementia, and 21 as having atypical parkinsonian syndromes. The PPV of the clinical diagnosis for the whole group was 89.4% (143/160); for idiopathic Parkinson's disease, 94.2% (131/139); for PSP, only 50% (4/8); for MSA, 57.1% (4/7); and for vascular parkinsonism, 66.7% (4/6). The sensitivity for idiopathic Parkinson's disease was 94.2% owing to eight false positive cases, mainly dementia with Lewy bodies (DLB), and two cases of PSP.

The diagnostic accuracy of 89.4% for the whole cohort was higher than in the group described by Hughes *et al* (85.3%),[2] and was similar to that of our own total group of 260 parkinsonian cases without and with dementia, where the rate of false clinical diagnosis was 11.5 % (table 2). This was lower than in previous clinicopathological series from the same hospitals and the same neuropathology department (table 2).

It is of interest that the majority of cases with a false clinical diagnosis of idiopathic Parkinson's disease in our cohort had a final pathological diagnosis of DLB—mainly "pure" DLB cases which often initially present with parkinsonism.[9 10] These were not included or mentioned in either of the British series.[1 3 6 7] In our recent consecutive necropsy series of 260 parkinsonian cases, DLB accounted for around 20% which, owing to improved neuropathological techniques and knowledge, was much higher than in previous series (table 1). The reason for the differences between the British series and our own is a matter for debate.

The recent British studies and our own studies imply that neurologists with particular expertise in the field of movement disorders may be best at recognising the clinical syndromes of parkinsonism. However, they also show clearly that neuropathological examination using modern immunohistochemical methods still represents the gold standard for the final diagnosis which, even after examination of the patients by very experienced clinicians, may differ by around 10% from the final clinical diagnosis. Improvement in the clinical consensus criteria and expertise may further reduce the rate of false clinical diagnosis of these devastating disorders—a possible basis for further improvements in treatment strategies.

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Smoking and cognitive change from age 11 to age 80

Age related cognitive decline affects people's quality of life and their ability to live independently.[1] A recent review stated, "[we] are aware of no studies on the relationship between smoking and cognitive decline associated with normal aging or studies of the effect of smoking on cognition in normally aging individuals."[1] Some previous studies examined smoking in relation to pathological cognitive aging, but lacked cognitive data before the initiation of smoking, and used crude clinical cognitive assessments.[2–4] Among middle aged subjects, current smoking was associated with poorer cognitive performance on tasks of psychomotor speed and cognitive flexibility.[5] Smoking has been identified as a possible risk factor for accelerated cerebral degenerative changes, cognitive decline, and dementia.[6] Here we show that smoking contributes to normal cognitive change from age 11 to age 80.

Participants, methods, and results

The Scottish Mental Survey of 1932 (SMS1932) tested mental ability in people born in 1921 (n = 87 498). The SMS1932's Moray House test (MHT) was validated against the Stanford Binet test and includes verbal reasoning, numerical, spatial, and other items. From 1999 to 2001 we traced and retested 550 people from Edinburgh who were born in 1921 (the Lothian birth cohort 1921). All lived independently. We excluded people with mini-mental state examination scores below 24 and those with known dementia. We traced their scores on the MHT from SMS1932, readministered the MHT using the same instructions and time limit as the SMS1932, and collected information on smoking. In all, 470 people (194 men) provided full data.

We examined the effect of smoking on cognitive change from age 11 to age 80 using general linear modelling (analysis of covariance; SPSS version 11). Age corrected MHT score at age 80 was the dependent variable, smoking (never (n = 205); current (n = 34); ex-smoker (n = 231)) and sex were between subject variables, and age corrected MHT score at age 11 was a covariate. Among the current smokers the mean (SD) age at starting smoking was 18.9 (5.5) years (range 9 to 40). The ex-smokers' mean age at starting smoking was 18.2 (5.2) years (range 7 to 60), and the mean age at stopping smoking was 49.6 (16.1) years (range 19 to 79 years). Only six of these ever-smokers (current and ex-) began smoking before the age of 11. The mean (SD) MHT scores for each smoking related subgroup at age 11 and age 80 are shown in table 1. MHT scores at age 11 had a large effect on scores at age 80 ($F_{1,463} = 332.2$, $p < 0.001$, $\eta^2 = 0.418$). There was a significant, independent effect of smoking ($F_{2,463} = 3.3$, $p = 0.039$, $\eta^2 = 0.014$), but not of sex